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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,029	12/16/2005	Sally-Anne Stephenson	2381.0010000/MAC	9023

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EXAMINER	
HALVORSON, MARK	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
09/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,029	STEPHENSON, SALLY-ANNE	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-12,14-19 and 21-38* is/are pending in the application.

4a) Of the above claim(s) *22-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-12, 14-19 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 7/10/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-12, 14-19 and 21-38 are pending.

Claims 22-38 have been withdrawn.

Claims 1-5, 7-12, 14-19 and 21 are currently under examination.

Objections to Specification withdrawn

The objections to the specification are withdrawn in view of Applicant's arguments and the amendments to the Specification.

- 35 USC § 112 2nd paragraph rejection withdrawn

The rejection of claims 76-87,89-91, 126 and 127 for being indefinite is withdrawn in view of the cancellation of claims 76-87,89-91, 126 and 127.

35 USC § 112 1st paragraph rejection maintained

The rejection of claims 1-5, 7-12, 14-19 for failing to comply with the enablement requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They

include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to a method for inhibiting the proliferation of a cancer cell, inducing the death of a cancer cell and treating or preventing cancer in a subject comprising contacting the cells with an antibody to an epitope on EphB4. The claims read on a method of preventing or treating cancer in a subject.

The specification discloses that EphB4 expression was upregulated on colon and breast cancer cells. (Example 1) The specification also discloses that polyclonal antibodies to EphB4 induced cell death in breast and colon cancer cell lines. (Example 3). The specification further discloses that cell death by the polyclonal antibodies is inhibited by specific EphB4peptides. (Fig 14). The specification does not disclose any in vivo studies on the treatment of cancer with antibodies to EphB4.

Applicants argue that the use of antibodies in the treatment of cancers is well known in the art and cite Bodey, Hudson and Cragg et al. However, as previously stated White et al discloses that numerous obstacles must be overcome for successful immunotherapy. These include choice of target antigen, immunogenicity of the antibodies, length of half-life and ability to recruit effector functions and antibody manufacturing. In regards to the choice of antigen Noren et al (cited previously) disclose that the Eph receptors are present on most tissues. (page 3994, 1st column). As recently as 2007, Noren stated that it is unknown if EphB4 therapeutic will be effective in the treatment of cancer. (page 3007, 2nd column). Furthermore, Bodey states the employment of mAbs in the treatment of human cancer is still in its infancy (page 611 2nd column). Furthermore, the antibodies that are presently being used in cancer trials are primarily monoclonal antibodies.

Applicants also argue that in vitro screen was fully established and had replaced the in vivo screens. Applicants also argue that the present inventors used an in vitro screen substantially equivalent to the in vitro screen described above to test the

antibodies to EphB4. However, it is noted that the in vitro screen has not replaced in vivo screens, in general. The NCI, which screen compounds for cancer researches, uses an initial in vitro screen using a panel of 60 cell lines to test primarily small molecules and natural product extracts for their potential anti-cancer effect. It is not evident that the in vitro screen was ever used to test for the use of antibodies in cancer therapy.

Applicant also indicate that US 20050084873 presents data showing that antibodies targeting epitopes in the extracellular domain of EphB4 not only inhibit tumor growth but cause regression of established tumors in a xenograft mouse model of a head and neck cancer. However, the results in US 20050084873 are not commensurate in scope with the claims as currently amended, of the present application. Applicants are claiming all cancer while 20050084873 used an animal model for head and neck squamous cell carcinomas. In addition, the example noted by applicants in 20050084873 demonstrated the treatment of the animal model for head and neck cancer with a specific monoclonal antibody against EphB4, G250, whereas applicants are claiming antibodies to specific regions of he EphB4 protein. The epitope recognized by G250 was not indicated in 20050084873.

Summary

Claims 1-5, 7-12, 14-19 and 21 stand rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Halvorson
Patent Examiner
571-272-6539

/MISOOK YU/
Primary Examiner, Art Unit 1642